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09/523,066	03/10/2000	Timothy P. Tully	1314.1058-0001	4462

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EXAMINER	
FORMAN, BETTY J	
ART UNIT	**PAPER NUMBER**
1634	14

DATE MAILED: 04/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/523,066	Applicant(s) TULLY ET AL.	
	Examiner BJ Forman	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 15-26* is/are pending in the application.

4a) Of the above claim(s) *1-10 and 16-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-15 and 24-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

FINAL ACTION

1. This action is in response to papers filed 7 February 2002 in Paper No. 13 in which claims 11, 15 and 24 were amended and claim 14 was canceled. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action of Paper No. 10 dated 13 July 2001 under 35 U.S.C. 112, second paragraph are withdrawn in view of the amendments. The previous rejections under 35 U.S.C. 103(a) are maintained. All of the arguments have been thoroughly reviewed and are discussed below.

The examiner's Art Unit has changed from 1655 to 1634. Please address future correspondence to Art Unit 1634.

Currently claims 11-13, 15 and 24-26 are under prosecution.

Information Disclosure Statement

2. The references listed on the 1449 and the International Search Report received 8 January 2002 in Paper No.11 have been reviewed. A copy of the initialed 1449 is enclosed with this action.

Restrictions

3. The Petition filed under 37 C.F.R. 1.144 is acknowledged and will be considered.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary

skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 11-15 and 24-26 are rejected under 35 U.S.C. 103(a) as being obvious over Yin et al. (Cell, 1994, 79: 49-58) in view of Ramsey, G. (Nature Biotechnology, 1998, 16: 40-44) and Tully et al. (U.S. Patent No. 5,929,223, filed 7 October 1994).

Regarding Claim 11, Yin et al. teach a method of identifying a gene involved in transcription-dependent memory comprising: training Drosophila to induce transcription-dependent memory formation in said Drosophila i.e. spaced training, (page 50, last paragraph—page 51-first paragraph); extracting RNA from head tissue of said trained Drosophila; hybridizing the RNA to DNA sequences via Northern Blot from a gene of the Drosophila genome i.e. dCREB2-b cDNA, under conditions appropriate for hybridization wherein a signal is produced upon hybridization and detecting the signal produced (page 56, last paragraph) and performing a statistical comparison between the signal detected and a signal detected in a control (page 51, left column, last line-right column, first paragraph). Yin et al. teach training control Drosophila under conditions insufficient to induce transcription-dependent memory i.e. massed training (page 55, right column. second full paragraph) and performing statistical comparisons between the trained Drosophila. Yin et al. also teach a comparison of hybridization signal between Drosophila trained to induce transcription-dependent memory and Drosophila trained insufficiently to induce transcription dependent memory i.e. in the absence of training (page 50, last paragraph and Fig. 1). Yin et al. teach that the cAMP signal transduction pathway is critically involved with memory events and the pathway involves numerous cAMP response genes including transcription factors and they teach that drugs that interfere with transcription or translation disrupt memory. These teachings suggest that memory events require de novo gene expression and that numerous genes are involved with the memory events (page 79, left column, last paragraph-right column first full paragraph) and while they teach hybridization via Northern Blot to compare expression, they do not teach synthesizing DNA probes from the extracted RNA and exposing

the DNA probes to microarray chips containing DNA sequences from genes of the Drosophila genome. However, microarrys comprising DNA sequences derived from extracted RNA was well known in the art at the time the claimed invention was made as taught by Ramsey. Specifically, Ramsey teaches a method to identify a gene or genes involved in transcription-dependent response comprising extracting RNA, synthesizing labeled cDNA probes from the RNA, hybridizing the DNA probes to microarray chips, detecting the signal produced, and performing a statistical comparison between the experimental and control (page 41, left column, last paragraph-right column) and they teach the method has been used in numerous model organisms e.g. plants, yeast, *S. cerevisiae, S. pneumoniae, E. coli* and has proven useful for large-scale, rapid identification of expression-specific genes (page 41, left column, last paragraph) wherein the array method was 10 time more sensitive than Northern Blots (page 41, right column last paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the northern blot gene identification of Yin et al. with the microarray identification exhibiting 10 fold sensitivity when compared to Northern Blots as taught by Ramsey wherein multiple response-specific genes are identified for the expected benefit of large-scale, rapid identification of expression-specific genes as taught by Ramsey (page 41, left column, last paragraph).

Regarding Claim 12, Yin et al. teach the method wherein transcription-dependent memory formation is long term memory formation (page 49, last paragraph-page 50, right column first full paragraph).

Regarding Claim 13, Yin et al. teach the method wherein transcription-dependent memory formation is induced using a spaced training protocol (page 50, last paragraph-page 51, first paragraph. Additionally, Yin et al. teach the conditions of a massed training protocol (page 55, right column, first full paragraph, lines 24-29). Yin et al. do not teach the method wherein the hybridization signals from the spaced trained and massed trained Drosophila are compared. However, Tully et al. teach a similar method comprising: training two groups of

Drosophila, one under conditions to induce transcription-dependent memory and a second under condition insufficient to induce transcription-dependent memory, extracting RNA from head tissue of both groups, hybridizing the RNA to DNA sequences from genes of the Drosophila and comparing the hybridization signals between the two groups (Column 25, lines 6-30). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the RNA analysis of Yin et al. wherein hybridization signals from trained and untrained Drosophila are compared to further compare hybridization signals from Drosophila following the different training protocols as taught by Tully et al. for the obvious benefit of analyzing training-specific expression to thereby identify memory-specific expression.

Regarding Claim 14, Yin et al. teach the conditions sufficient to induce transcription-independent memory formation but not transcription-dependent memory formation i.e. massed training (page 55, right column, first full paragraph, lines 24-29).

Regarding Claim 15, Yin et al. teach transcription-independent memory formation is induced using a massed training protocol (page 55, right column, first full paragraph, lines 24-29).

Regarding Claim 24, Yin et al. teach a method of identifying a gene involved in transcription-dependent memory comprising: training Drosophila to induce transcription-dependent memory formation in said Drosophila i.e. spaced training, (page 50, last paragraph—page 51-first paragraph); extracting RNA from head tissue of said trained Drosophila; exposing the RNA to DNA sequences from a gene of the Drosophila genome i.e. dCREB2-b cDNA, under conditions appropriate for hybridization wherein a signal is produced upon hybridization, detecting the signal produced, comparing the signal to the signal from control Drosophila (page 56, last paragraph) and performing a statistical comparison between the signal detected and a signal detected in a control (page 51, left column, last line-right column, first paragraph). Yin et al. teach that the cAMP signal transduction pathway is critically involved with memory events and the pathway involves numerous cAMP response

genes including transcription factors and they teach that drugs that interfere with transcription or translation disrupt memory. These teachings suggest that memory events require de novo gene expression and that numerous genes are involved with the memory events (page 79, left column, last paragraph-right column first full paragraph) and while they teach hybridization via Northern Blot to compare expression, they do not teach synthesizing DNA probes from the extracted RNA and exposing the DNA probes to microarray chips containing DNA sequences from genes of the Drosophila genome they do not teach synthesizing DNA probes from the extracted RNA and exposing the DNA probes to microarray chips containing DNA sequences from genes of the Drosophila genome. However, microarrys comprising DNA sequences derived from extracted RNA was well known in the art at the time the claimed invention was made as taught by Ramsey. Specifically, Ramsey teaches a method to identify a gene or genes involved in transcription-dependent response comprising extracting RNA, synthesizing labeled cDNA probes from the RNA, hybridizing the DNA probes to microarray chips, detecting the signal produced, and performing a statistical comparison between the experimental (page 41, left column, last paragraph-right column) and they teach the method has been used in numerous model organisms e.g. plants, yeast, *S. cerevisiae, S. pneumoniae, E. coli* and has proven useful for rapid identification of expression-specific genes (page 41, left column, last paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the northern blot gene identification of Yin et al. with the microarray identification exhibiting 10 fold sensitivity when compared to Northern Blots as taught by Ramsey wherein multiple response-specific genes are identified for the expected benefit of large-scale, rapid identification of expression-specific genes as taught by Ramsey (page 41, left column, last paragraph).

Regarding Claim 25, Yin et al. teach the method wherein said transcription-dependent memory formation is long term memory formation i.e. spaced training (page 51, left column, first paragraph).

Regarding Claim 26, Yin et al. teach the method wherein said transcription-dependent memory formation is induced using a spaced training protocol (page 51, left column, first paragraph).

Response to Arguments

6. Applicant argues that Yin et al do not teach or suggest use of microarray chips to identify genes involved in transcription-dependent memory function and they do not teach or suggest the use of a statistical comparison between signals detected from the chip. The arguments have been considered but are not found persuasive because Yin et al teach performing a statistical comparison between the signals detected (page 51, left column, last line-right column, first paragraph). While Yin et al do not teach use of a microarray chip and statistical comparisons of signals obtained there from, Ramsey specifically teaches a method to identify a gene or genes comprising extracting RNA, synthesizing labeled cDNA probes from the RNA, hybridizing the DNA probes to microarray chips, detecting the signal produced, and performing a statistical comparison between the experimental (page 41, left column, last paragraph-right column). Therefore, it is the combination of Yin et al and Ramsey that makes the claimed invention obvious because it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the northern blot gene identification of Yin et al. with the microarray identification exhibiting 10 fold sensitivity when compared to Northern Blots as taught by Ramsey wherein multiple response-specific genes are identified for the expected benefit of large-scale, rapid identification of expression-specific genes as taught by Ramsey (page 41, left column, last paragraph).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues that Tully et al do not teach or suggest use of microarray chips to identify genes involved in transcription-dependent memory function and they do not teach or suggest the use of a statistical comparison between signals detected from the chip. The argument has been considered but is not found persuasive because the rejection over Tully et al of Paper No. 7 was withdrawn in the rejection of Paper No. 10. Therefore, the arguments are deemed moot in view of the fact that the arguments do not address the instant rejection.

Applicant argues that Ramsey does not teach or suggest performing a gene chip identification of those genes expressed during transcription-dependent memory function but not during transcription-independent memory function. Applicant further argues that the rejection is improper because the examiner has not identified a suggestion in the prior art for combining the teaching of Ramsey with that of Yin et al.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Yin et al teach identification of a gene or genes involved in transcription-dependent memory and differ from the instantly claimed invention only in that Yin et al do not perform their hybridization on a microarray. While Yin et al do not teach use of a microarray, Ramsey specifically teaches a method to identify a gene or genes comprising extracting RNA, synthesizing labeled cDNA probes from the RNA, hybridizing the DNA probes to microarray chips, detecting the signal produced, and performing a statistical comparison between the experimental (page 41, left column, last paragraph-right column) and the arrays have been used for gene-expression analysis and gene identification in numerous model organisms e.g. plants, yeast, *S. cerevisiae, S. pneumoniae, E. coli* and has proven useful for rapid identification of expression-specific genes (page 41, left column, last paragraph) which clearly suggest that microarray hybridization is useful for universal gene identification. Therefore, the teaching of Ramsey would have clearly suggested to one skilled in the art to apply the microarray hybridization to gene expression analysis and identification for the obvious benefits of large-scale, rapid identification of expression-specific genes as taught by Ramsey (page 41, left column, last paragraph).

Therefore, it is the combination of Yin et al and Ramsey that makes the claimed invention obvious because it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the northern blot gene identification of Yin et al. with the microarray identification exhibiting 10 fold sensitivity when compared to Northern Blots as taught by Ramsey wherein multiple response-specific genes are identified for the expected benefit of large-scale, rapid identification of expression-specific genes as taught by Ramsey (page 41, left column, last paragraph).

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Patent Examiner
Art Unit: 1634
April 4, 2002

W. Gary Jones
Supervisory Patent Examiner
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